

EXHIBIT 51

The Cuyahoga County Heroin Epidemic

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ABSTRACT: Cuyahoga County, Ohio has recently seen a dramatic rise in the number of deaths associated with heroin (DAH). DAH rose from 40 in 2007 to 161 in 2012 with heroin now identified in half of all overdose deaths. One third of DAH involve heroin alone; the remainder, in combination with other drugs. Over this period, opioid pain reliever (OPR) deaths appear to have plateaued.

Along with this rise have been shifts in overdose victim demographics. These data most notably include a rise in the number of women (from 15% to 24%), overdoses between the ages 19 and 29 (8% to 25%), and a generally equal number of urban and suburban fatalities.

The Medical Examiner's Office conducted a retrospective analysis of 2012 fatalities to identify potential risk factors and intervention points. This review indicates that most victims (81%) were known to abuse drugs. Half were found with drug paraphernalia at the scene. Approximately 12% were using heroin with other addicts, while 60% were using drugs or succumbed to them in proximity to other non-using people. Emergency medical services were only able to administer naloxone in 22% of cases. Histories of recent abstinence (29%), incarceration (18%), and detoxification (31%) were noted and may reflect times of increased risk secondary to decreased tolerance. A prescription for legal controlled substances was noted in 64% of DAH (the most common medications being OPRs and benzodiazepines). This suggests a need to address prescribing practices. Public health interventions, implemented or planned, based on these data are discussed.

KEYWORDS: Forensic pathology, Public health, Heroin, Opioid pain reliever

INTRODUCTION

The United States is in the midst of a significant upward trend in mortality associated with accidental deaths due to prescription opioid pain relievers (OPR) (1, 2). More recently in Cuyahoga County (metropolitan Cleveland), we have observed a substantial increase in overdose deaths associated with heroin (DAH), either alone or in combination with other drugs. At the same time, OPR deaths appear to have plateaued after a less dramatic rise, suggesting a transition from OPR to heroin in fatal overdoses. Drug abuse trends vary over time and region but this evolution in our local narcotic abuse pattern may be a harbinger of a national public health problem as efforts continue to address OPR abuse. This paper presents the data from Cuyahoga County with regard

to the heroin epidemic. It also includes information from a more in-depth analysis performed to identify areas of possible intervention that may be useful to other jurisdictions where this problem already exists or becomes a reality in the future.

MATERIALS AND METHODS

Medical Examiner case files were reviewed from 2007 to 2012 to identify DAH. Deaths due to heroin alone or in combination with other drugs were included for study. Basic demographic data regarding age, gender, race, and residency status (Cleveland vs. suburb) were recorded.

In response to the rising death toll associated with heroin, a multidisciplinary poison death review

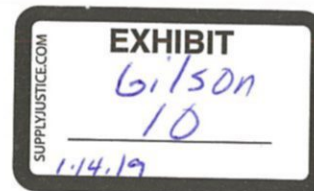
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committee (PDRC), chaired by the Medical Examiner, was assembled to provide in-depth data to inform policy decisions. The Medical Examiner's Office undertook a retrospective review of the 161 fatalities from 2012 and, with the PDRC, continues to prospectively review 2013 deaths. One stillbirth with polypharmacy intoxication was excluded from the 2012 in-depth death review. The remaining 2012 deaths form the basis of this report.

The 2012 DAH were analyzed to identify if the decedent was known to have been using drugs with others, if others were present but not using drugs where the decedent overdosed or proceeded through the terminal stages of intoxication, whether first responders administered naloxone, if drug paraphernalia (e.g., syringes, spoons, packets with powder, etc.) was present at death scene, if the decedent had a history of previous illicit drug use, if the decedent had a history of intravenous drug use, previous medical treatment within two years of death, previous detoxification treatment within two years of death, previous incarceration within two years of death, and if there was a reported period of abstinence shortly before death.

The relevant information from the 2012 DAH was compared with de-identified data from the county needle exchange program to enumerate needle exchange program participants who subsequently overdosed with heroin. Similarly, the 2012 DAH database was compared with de-identified data from the Ohio Automated Rx Reporting System (OARRS), the Ohio prescription drug monitoring program. This permitted identification of legal prescriptions for controlled substances, including OPR in individuals who subsequently went on to overdose from heroin. OARRS maintains data for two years, generating a retrospective analysis of legal prescriptions among the 2012 DAH, which only ranged from 6-18 months.

RESULTS

Heroin mortality rose significantly from 2007, when there were 40 DAH, to 2012, when there were 161. Cocaine mortality did not show a similar trend and the rise in mortality associated with oxycodone, the most common lethal OPR in our jurisdiction for the entire study period, was quantitatively less (Table 1). Small, interchangeable variations in mortality associated with other OPR were observed in our jurisdiction during the study period. Overall OPR mortality mirrored oxycodone so this is presented as a proxy for OPR mortality trends since these trends were largely driven by oxycodone.

Year	Heroin	Cocaine	Oxycodone
2012	161	108	32
2011	107	94	34
2010	91	97	36
2009	64	112	36
2008	64	102	21
2007	40	98	13

	2007 N=40	2012 N=161
White	30 (75.00%)	139 (86.88%)
Male	34 (85.00%)	122 (75.75%)
Female	6 (15.00%)	39 (24.25%)
Age 19-29	3 (7.50%)	41 (25.63%)
Age 45-60	30 (80.00%)	63 (39.38%)
Age 60+	2 (5.00%)	6 (3.75%)
Suburban residency*	17 (42.50%)	71 (44.38%)

*Not including non-county residents.

Deaths due to heroin intoxication alone (versus mixed intoxications) are not routinely tracked at our office but in 2012 represented 33% of DAH. Whites continued to account for the majority of DAH with a slight rise over this time period (75% to 87%). The percentages of women and young adults (ages 19-29) rose over this time period from 15% to 24% and 8% to 25% respectively. However, the typical profile remains males in the 45-60 age range. Residency status (urban Cleveland versus suburban county) showed a nearly even split throughout the study period (Table 2).

Analysis of the 2012 DAH revealed that 12% were using drugs with other people while 59% died in proximity to others who were not using drugs. Emergency medical services responded to the vast majority (95%) of cases but administered naloxone in only 22%. Scene investigation revealed the presence of drug paraphernalia in 50% of cases (Table 3).

Factor	Number	Percentage
History of illicit drug use	129	80.63%
History of intravenous drug use	78	48.75%
Period of abstinence	46	28.75%
Incarceration	29	18.13%
Detoxification treatment	49	30.63%
General medical treatment	75	46.88%
Emergency medical services response	152	95.00%
Naloxone administered	36	22.50%
Using drugs with others	19	11.88%
Others present, not using drugs	94	58.75%
Paraphernalia found at scene	81	50.63%

Most (81%) of DAH had a previous history of illicit drug use, usually heroin. Intravenous drug abuse was reported in just under half (49%) of DAH. A period of abstinence from heroin was reported in 29% of DAH. This ranged from voluntary efforts to involuntary interventions like hospitalization and incarceration. Incarceration within two years of death was noted in 18% of DAH and previous detoxification treatment over the same period was noted in 31% of cases. General medical treatment of any kind was sought by 47% of DAH victims within two years of death (Table 3).

Comparison between the records from the needle exchange program and the medical examiner database revealed that 8/160 (5%) were enrolled in the program.

Of the 160 DAH in 2012, 102 (64%) had a file in the prescription drug monitoring program. Of these, the majority (87/102, 85%) was for OPR (suboxone not included). Just under half (49/102, 48%) had a prescription for a benzodiazepine sedative (zolpidem not included). The most common OPR were oxycodone, hydrocodone, and tramadol. The most common benzodiazepines were alprazolam, diazepam, lorazepam, and clonazepam. Of individuals with a legal OPR prescription, most (71%) had multiple prescriptions and this was also true to a slightly lesser extent (67%) for the benzodiazepines (Table 4). The OARRS data were de-identified with regard to prescriber, so "doctor-shopping" (more than five prescribers of controlled substances within a one year period) could not be assessed for the 2012 overdoses.

Data	N=160
Record on file in OARRS	102 (63.75%)
Prescription for opiate pain relievers (OPR) in OARRS (suboxone not included; n=102)	87 (85.29%)
Multiple prescriptions for OPR (n=87)	62 (71.26%)
Prescription for benzodiazepine in OARRS (zolpidem not included; n=102)	49 (48.04%)
Multiple prescriptions for benzodiazepine (n=49)	33 (67.35%)

DISCUSSION

OPR have recently assumed a large role in mortality attributable to accidental overdose in association with substance abuse (3). Our results in Cuyahoga County indicate that, while OPR deaths have risen in recent years, the most dramatic rise in accidental drug deaths has been due to heroin. As DAH in Cuyahoga County have risen, our data indicate that OPR deaths appear to have reached a plateau. This suggests that the addicted population may be transitioning to heroin, possibly for cost and/or availability reasons. Little evidence has been published documenting transitions from OPR to heroin (4), but given the similar pharmacologic effects of the two, this shifting trend in mortality is disturbing and requires further monitoring on a national level.

As noted above, there is a dearth of firm evidence establishing the role of OPR as a gateway to heroin (4). Our prescription drug monitoring program data clearly establish a link between OPR use and DAH, but it is unclear whether this represents evidence of a transition between OPR and heroin or simply reflects an addict population that uses these substances interchangeably. Concerns have been raised about the increasing frequency with which OPR are prescribed (5, 6) and our data support those concerns. OARRS offered a very limited "look back" for this study; the State of Ohio does not require universal entry of prescribed controlled substances into the OARRS database. Even with these limitations, most DAH fatalities had access to legal controlled substances and, of those with access, the majority were recipients of multiple prescriptions. Since the majority of DAH in our study consisted of individuals known to abuse drugs, it can only be concluded that there is a failure to identify these individuals at risk to die from heroin overdose on the part of some prescribers. Addressing these issues of OPR over-distribution

and distribution to at risk individuals will likely require extensive re-education in prescribing practices.

The most common age group for DAH is 45-60 years, which is consistent with previous observations (7, 8) that heroin overdose is not usually a problem confined to novice users. Our data indicate a rapid growth in DAH in the 19-29 year old age group but, in general, most (81%) of DAH were in individuals with a known history of drug abuse and the younger age group were no exception. Whites accounted for most DAH and males were more likely to overdose than women, although an upward trend for women was noted over the study period. This mirrors a national trend in OPR mortality (9) and warrants further study as evidence of the possibility of transitioning from OPR to heroin. We also observed a fairly even division between residency in the city of Cleveland and the suburban communities in our jurisdiction. This was unexpected in our county and indicates that the traditional model of heroin addiction as an inner-city problem and OPR addiction as a more suburban or rural one is no longer applicable. Finally, the large percentage of intravenous drug use and the 2:1 ratio of mixed drug intoxications including heroin (versus intoxication with heroin alone) points to the increased lethality of intravenous use and polysubstance abuse, as has been described previously (10).

In addition to basic monitoring as to cause of death, we suggest that a more comprehensive review of medical examiner/coroner death investigation data may be a very beneficial initial course of action in the identification of intervention points to decrease mortality. While demographic data alone suggest targeted interventions such as public service announcements tailored to specific age groups, it is likely that detailed review supplemented by additional investigators will identify additional risk factors and potential strategies. The creation of a PDRC facilitates further in-depth analysis by providing primary information from first-hand sources in the medical, legal, justice and public health systems. It also permits rapid dissemination of information to a number of interested stakeholders and can serve to integrate the medical examiner/coroner into the local public health community on this and other critical issues. By a more thorough analysis of 2012 DAH data, we identified a substantial gap between the number of decedents who received naloxone, an antidote for opiate/opioid intoxication, and the number of individuals whose deaths occurred in proximity to others (either while using drugs with others (12%) or in the company of others present who were not using drugs (59%)). It is uncertain what impact the administration

of naloxone by these bystanders would have had on overall mortality, but this large disparity strongly suggests the potential benefit of more widespread availability of naloxone through a lay naloxone distribution program, similar to that introduced with success in other cities (11). Cuyahoga County introduced such a program in March 2013. The program uses the county free clinic (where needle exchange occurs) and health department offices as sites for distribution. Although very few (5%) of 2012 DAH decedents were enrolled in the needle exchange program, this approach offered access to a large population of addicts. Involvement in treatment programs exhibits a protective effect against overdose mortality (8), so it is not surprising that the number of needle exchange enrollees who died of heroin overdose is low. The interaction of these addicts with others (who may not be enrolled) may offer the benefit of raising initial awareness within the population of the availability of naloxone.

In our study, a period of abstinence was noted in 29% of DAH. Abstinence produces a loss of tolerance and increases the likelihood of fatal overdose. There are inherent potential limitations in accepting undocumented reports of abstinence and the actual incidence of this risk factor is difficult to gauge accurately. Coupled with our associations of DAH with recent incarceration (18%) and dependency treatment (31%), it would seem that educational intervention with at risk populations regarding the relationship of abstinence/loss of tolerance and mortality is worth pursuing. To that end, all inmates leaving Cuyahoga County correctional facilities receive a letter from the Medical Examiner's Office addressing this issue. Wider distribution of this letter into treatment centers is currently under consideration.

Drug paraphernalia is found at the scene of death in 50% of DAH. Since the delay associated with toxicological confirmation of heroin overdose may impede law enforcement investigation, the PDRC suggested that an early warning system be developed to alert specialized drug task forces within police departments and the prosecutor's office as to potential of a DAH based on the presence of paraphernalia. This recommendation has been recently implemented with the medical examiner death scene investigator serving as the point person to confirm the presence of paraphernalia and issue the alert.

In summary, we report an increase in opioid/opiate mortality with evidence suggesting a transition from OPR to heroin. We also define a potential public health role for the medical examiner/coroner in an emerging public health crisis to include both data provision as well as participation in policy decision-making for intervention.

DISCLOSURES

This work was presented at the 2013 Annual Meeting of the National Association of Medical Examiners. The authors, reviewers, editors, and publication staff do not report any relevant conflicts of interest.

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